Notice of Allowability	Application No.	Applicant(s)	
	10/675,765	NGUYEN ET AL.	
	Examiner	Art Unit	
	Yelena G. Gakh, Ph.D.	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *amendment filed on 06/09/08*.

2. ☒ The allowed claim(s) is/are *31,33,36-41,43,46,48,51-56 and 58*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Hoa D. Nguyen on 08/13/08.

The application has been amended as follows:

Rejoin claims 46-60.

Cancel claims 32, 34-35, 42, 44-45, 47, 49-50, 57 and 59-60.

Claim 31. (Amended) A method of ~~synthesis of stable isotope labeled internal standard and additional derivatizing reaction in the identification and~~ quantification of alcohol(s) in a sample comprising the steps of:

a) synthesizing a stable isotope labeled ester internal standard of said alcohol, wherein the ester is selected from a group consisting of R_1OCOR_4, $R_1CH_2OCOR_4$, $R_1R_2CHOCOR_4$, and $R_1R_2R_3OCOR_4$, where R_1, R_2, and R_3 are alkyl, aryl, and heteroatom containing cyclic or non-cyclic groups, and R_4 is a stable isotope labeled alkyl or aryl group, by reacting an authentic sample of said alcohol with a stable isotope labeled reagent;

~~a)~~ b) combining a known amount of ~~a~~ the synthesized stable isotope labeled ester internal standard of said alcohol with said sample comprising said alcohol ;

~~b)~~ c) contacting said combined sample and the internal standard with an acid anhydride or an acid chloride to quantitatively convert said alcohol in said sample into an ester of identical structure as that of said stable isotope labeled ester internal standard except for the stable isotope atoms, wherein there is no conversion of said stable isotope labeled ester internal standard to its corresponding non-labeled ester compound;

~~c)~~ d) extracting ~~said sample to isolate~~ said ester and said stable isotope labeled ester internal standard from said combined sample; ~~and~~

~~d)~~ e) ~~analyzing~~ quantifying said ester by isotope dilution mass spectrometric method using ~~and~~ said stable isotope labeled ester internal standard; ~~by mass spectrometry.~~ and,

f) calculating the amount of said alcohol in said sample from the amount of said ester.

Claim 33. (Amended) The method of claim 31 wherein said alcohol ~~is an organic chemical of~~ has molecular mass less than 1000 atomic unit and is selected from the group consisting of ~~having the following formula~~ R_1OH, R_1CH_2OH, R_1R_2CHOH, $R_1R_2R_3COH$, wherein R_1, R_2, and R_3 are alkyl, aryl, and heteroatom containing cyclic or non-cyclic groups ~~and wherein OH is a hydroxyl group~~.

In **Claim 36**: replace [35] with -- 31 --.
In **Claim 37**: replace [e)] with -- d) --.

Claim 40. (Amended) The method of claim ~~31~~ 39 wherein said ~~multiple~~ plurality of alcohols can be converted to ~~said~~ multiple esters using ~~either~~ a single acid anhydride or a single acid chloride.

Claim 41. (Amended) The method of claim ~~31~~ 39 wherein ~~multiple~~ a plurality of labeled ester internal standards can be synthesized from said plurality of alcohols using ~~either~~ a single labeled acid anhydride or a single labeled acid chloride.

In **Claim 43**: replace [b)] with -- c) --.

Claim 46. (Amended) A method of ~~identification and~~ quantification of alcohol(s) in a sample comprising the steps of:
a) synthesizing a stable isotope labeled carbamate internal standard of said alcohol, wherein the carbamate is selected from a group consisting of R_1OCONR_4, $R_1CH_2OCNR_4$, $R_1R_2CHOCONR_4$, and $R_1R_2R_3OCNR_4$, where R_1, R_2, and R_3 are alkyl, aryl, and heteroatom containing cyclic or non-cyclic groups, and R_4 is a stable isotope labeled alkyl or aryl group, by reacting an authentic sample of said alcohol with a stable isotope labeled reagent;
~~a)~~ b) combining a known amount of ~~a~~ the synthesized stable isotope labeled carbamate internal standard with said sample comprising said alcohol;

~~b)~~ c) contacting said combined sample and the stable isotope labeled carbamate internal standard with an isocyanate to quantitatively convert said alcohol in said sample into a carbamate of identical structure as that of said stable isotope labeled carbamate internal standard except for the stable isotope atoms, wherein there is no conversion of said stable isotope labeled carbamate internal standard to its corresponding non-labeled carbamate compound;

~~c)~~ d) extracting ~~said sample to isolate~~ said carbamate and said stable isotope labeled carbamate internal standard from said combined sample; ~~and~~

~~d)~~ e) ~~analyzing~~ quantifying said carbamate by isotope dilution mass spectrometric method using ~~and~~ said stable isotope labeled carbamate internal standard; ~~by mass spectrometry.~~ and

f) calculating the amount of said alcohol in said sample from the amount of said carbamate.

48. (Amended) The method of claim 46 wherein said alcohol ~~is an alcohol having the following formula~~ has molecular mass less than 1000 atomic unit and is selected from the group consisting of R_1OH, R_1CH_2OH, R_1R_2CHOH, $R_1R_2R_3COH$, wherein R_1, R_2, and R_3 are alkyl, aryl, and heteroatom containing cyclic or non-cyclic groups.

In **Claim 51**: replace [50] with -- 46 --.
In **Claim 52**: replace [c)] with -- d) --.
In **Claims 55 and 56**: replace [46] with -- 54 --.
In **Claim 58**: replace [b)] with -- c) --.

Claims 31, 33, 36-41, 43, 46, 48, 51-56 and 58 are allowed. The new numbering of claims is 1 through 18.

The following is an examiner's statement of reasons for allowance: the subject matter recited in the amended claims 31, 33, 36-41 and 43 is not disclosed or fairly suggested by the cited prior art.

The prior art related to carbamate derivatives is as following:

The closest prior art is that of *Aubry et al. (J. Agric. Food Chem. 1997)*, who teach "Quantitative Determination of Potent Flavor Compounds in Burgundy Pinot Noir Wines Using a Stable Isotope Dilution Assay". The method comprises using internal standards:

> "The deuteriated standards, ethyl-d_3 dihydrocinnamate (ethyl-d_3 phenyl-3-propionate) and ethyl-d_3 cinnamate (ethyl-d_3 phenyl-3-propenoate), further referred to as (A-d_3) and (B-d_3), were prepared from ethanol-d_3 and the suitable acyl chloride. The alcohol-d_3 (0.2 mL) in pyridine (1 mL) was added at 0 °C to a solution of acyl chloride (5 mmol) in pyridine (5 mL). The reaction mixture was then stirred at room temperature (RT) for 2 h and poured into 50 mL of 1 M HCl. The aqueous layer was extracted with ether (2 x 50 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$, dried over Na_2SO_4, and evaporated. The crude product was purified on silica gel (pentane/ diethyl ether, 80/20). Molar yield: 80-90%. Methyl-d_3 anthranilate (methyl-d_3 amino-2-benzoate) and ethyl-d_3 anthranilate (ethyl-d_3 amino-2-benzoate), further referred to as (C-d_3) and (D-d_3), were not prepared according to the classical method, as alcohol-d_3 was judged too expensive. They were synthesized from the mild hydrolysis of methyl-d_3 and ethyl-d_3-2-trifluoroacetamidobenzoates as described in Figure 1 (Errede et al., 1977)." (Page 2120, right column).

Thus, the method of preparation of internal standards is totally different from the method of the invention.

Woidich et al. (Mikrochim. Acta, 1989) teach "The Use of N-Alkylcarbamates in Sample Mapping of Terpene Alcohols". No internal standard is disclosed in the reference. *Quirke et al. (J. Nat. Prod. 2000)* disclose "Ferrocene-Based Electroactive Derivatizing Reagents for the Rapid Selective Screening of Alcohols and Phenols in Natural Product Mixtures Using Electrospray-Tandem Mass Spectrometry" (Title). The analysis included GC-MS analysis utilizing internal standards; however, the internal standards were nonane or hexadecane for analysis of essential oils. *Quirke et al. (J. Mass Spectrom., 2001)* teach "Electrospray tandem mass spectrometric study of ferrocene carbamate derivatives of saturated primary, secondary and tertiary alcohols" (Title). No internal standard is disclosed in the reference.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Yelena G. Gakh/
Primary Examiner, Art Unit 1797

8/14/2008